REMARKS

Reconsideration and withdrawal of the rejections set forth in the Office Action dated September 14, 2006 are respectfully requested.

I. Amendments

Claims 21 and 27 are amended to recite "consisting of" and to recite "from one to five." Basis for these amendments can be found on page 104, lines 22-36 and page 108, lines 28-34.

Claim 25 is amended for proper grammar.

Claim 28 is canceled without prejudice. Applicants reserve the right to pursue the canceled subject matter in this or a continuing application.

No new matter is added by way of these amendments.

II. Priority

Applicants enclose herewith a certified translation of priority application no. JP 2003-92923 filed on March 28, 2003. Applicants have complied with all the requirements under 35 U.S.C. § 119(a)-(d) for foreign priority. Accordingly, the present application is entitled to a priority date of March 28, 2003.

III. Claim Objections

Claim 28 was objected to as allegedly being in improper dependent form. In order to ease prosecution, claim 28 stands canceled without prejudice.

Claim 21 was objected to for the language "wherein the agent comprises a PTD domain" as allegedly informal claim language. Applicants have amended claim 21 in accord with the Examiner's kind suggestion.

Claim 25 was objected to for the language "wherein the agent capable of inhibiting the p75 signal transduction pathway the action of inhibition" for alleged grammatical errors. Applicants have amended claim 25 for proper grammar.

Accordingly, Applicants respectfully request withdrawal of the objections to the claims.

IV. Rejections Under 35 U.S.C. § 112, first paragraph

Claims 21-22, 25-28, and 263-266 were rejected under 35 U.S.C. §112, first paragraph as allegedly failing to comply with the written description requirement. Without acquiescing as to the Examiner's interpretation of the claims, Applicants have amended claims 21 and 27 to recite SEQ ID NO:2 and variants with one to five single amino acid additions, substitutions, or deletions. One skilled in the art would clearly recognize that the inventors were in possession of the full scope of the claimed genus. Accordingly, Applicants respectfully submit that these claims comply with the written description requirement.

Claims 21-22, 25-28, and 263-266 were further rejected under 35 U.S.C. §112, first paragraph as allegedly failing to comply with the enablement requirement. Applicants have amended claims 21 and 27 to recite SEQ ID NO:2 and variants with one to five single amino acid additions, substitutions, or deletions. It is well within the skill level of those in the art to make one to five single amino acid substitutions, additions, and deletions while retaining the biological activity of Pep5 without undue experimentation.

Applicants teach a variety of assays that one of skill the art can perform to verify that the amino acid change does not result in loss of peptide activity. Applicants teach that the activity of a Pep5 peptide, which binds to p75 and serves to inhibit Rho, can be measured "with a Rho activity assay which blocks activation of Rho by a myelin-derived protein, or the like" (see page 61, lines 23-34). Such assays include immunological assays and phosphorylation quantification (see page 175, lines 5-14). Furthermore, in Examples 2-6 through 2-9, Applicants disclose an *in vivo* nerve regeneration assay that can be performed using variants of Pep5 (see page 353, line 4 through page 354, line 8).

Accordingly, Applicants submit that the specification would enable any person skilled in the art to which it pertains to make and use the claimed invention.

In light of the above, Applicants submit that the present claims satisfy the requirements of §112, first paragraph and respectfully request that the rejections be withdrawn.

V. Rejections Under 35 U.S.C. § 102

Claims 21-22, 25-28, and 263-266 were rejected under 35 U.S.C. § 102(e) as allegedly anticipated by Bredesen (U.S. Patent Publication 2004/0192889).

These rejections are respectfully traversed for the following reasons:

A. The Present Claims

Claim 21 is directed to a composition for regenerating nerves, comprising an agent capable of inhibiting a p75 signal transduction pathway, wherein the agent is a Pep5 polypeptide consisting of the sequence of SEQ ID NO:2, or a sequence derived therefrom by from one to five amino acid substitutions, deletions, and additions which retains the biological activity of Pep5; and wherein the agent also comprises a PTD domain.

Claim 27 is directed to a composition for regenerating nerves comprising an agent capable of inhibiting a p75 signal transduction pathway, wherein the agent is a Pep5 polypeptide consisting of the sequence of SEQ ID NO:2, or a sequence derived therefrom by from one to five amino acid substitutions, deletions, and additions which retains the biological activity of Pep5; wherein the agent comprises a PTD domain; and wherein the composition is suitable for *in vivo* or *in vitro* administration forms.

B. The Applied Art

BREDESEN teaches a fusion protein containing the first helix of the intracellular domain of p75 coupled with the TAT protein.

C. Analysis

The standard for lack of novelty, that is, for anticipation, is one of strict identity. To anticipate a claim for a patent, a single prior source must contain all its essential elements. M.P.E.P. § 2131.

Bredesen fails to disclose at least a composition for regenerating nerves comprising a Pep5 polypeptide consisting of the sequence of SEQ ID NO:2 or sequence derived therefrom by one to five amino acid substitutions, deletions, or

additions as presently claimed. Bredesen makes no mention of a Pep5 polypeptide or sequence derived therefrom.

Accordingly, Applicants respectfully request withdrawal of the rejection under 35 U.S.C. §102.

VI. Rejections Under 35 U.S.C. § 103

Claims 21-22, 25-28, and 263-266 were rejected under 35 U.S.C. §103(a) as allegedly anticipated by Bredesen (U.S. Patent Application Publication 2004/0192889).

Claims 21-22, 25-28, and 263-266 were rejected under 35 U.S.C. §103(a) as allegedly obvious over Ilag *et al.* in view of Schwarze *et al.* (*Science*, 285:1569-1572, 1999), Voet *et al.* (Biochemistry, Second Edition, pp. 58–59, 1995), and Bertin *et al.* (U.S. Patent Publication 2002/0061833).

These rejections are respectfully traversed for the following reasons.

A. The Present Claims are described above.

B. The Applied Art

BREDESEN is described above.

ILAG ET AL. describe methods for identifying nucleic acid sequences which encode two or more specific interacting peptides or proteins.

SCHWARZE ET AL. describe fusion proteins that contain an NH_2-terminal 11-amino acid protein transduction domain (PTD) for transduction of proteins.

VOET ET AL. list the amino acids and their residue mass.

BERTIN ET AL. relate to a method for determining whether a test compound alters the binding of CARD-3 to p75.

C. Analysis

According to the M.P.E.P. § 2143, "to establish a *prima facie* case of obviousness, three basic criteria must be met. First there must be some suggestion

or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Third, the prior art references (or references when combined) must teach or suggest all the claim limitations."

1. Rejection over Bredesen

As noted above, Bredesen makes no mention of any Pep5 polypeptide. Nor would one modify the sequences as described in Bredesen as there is simply no guidance to do so.

2. Rejection over Ilag *et al.* in view of Schwarze *et al.*, Voet *et al.*, and Bertin *et al.*

The present claims are directed to a composition for regenerating nerves comprising an agent capable of inhibiting a p75 signal transduction pathway, wherein the agent is a Pep5 polypeptide or a sequence derived therefrom by defined parameters, wherein the agent also comprises a PTD domain. The cited references, alone or in combination, fail to show or suggest the claims as a whole, including the nature of the results obtained. Ilag *et al.* teach selection of a PE2 protein sequence by SIP. However, Ilag *et al.* makes no mention of a Pep5 sequence also comprising a PTD domain. None of the Schwarze *et al.*, Voet *et al.*, or Bertin *et al.* provides the missing teaching. Although Schwarze *et al.* teach fusion proteins containing an 11-amino acid PTD, this reference merely describes the introduction of the proteins into cells and provides no motivation or guidance for modification of a Pep5 polypeptide. Voet *et al.* merely gives some physical data for the amino acids. Bertin *et al.* teach a CARD-3 protein that is useful in inhibiting apoptosis and in the identification of compounds which modulate apoptosis and cannot provide motivation for modification of a Pep5 polypeptide.

Accordingly, Applicants respectfully request withdrawal of the rejection under 35 U.S.C. §103.

VII. Conclusion

In view of the foregoing, Applicants submit that the claims pending are in condition for allowance. A Notice of Allowance is, therefore, respectfully requested. If the Examiner has any questions or believes a telephone conference would expedite prosecution of this application, the Examiner is encouraged to call the undersigned at (650) 838-4410.

Respectfully submitted,
Perkins Coie LLP

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